

10/635 342

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Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 19:08:29 ON 24 SEP 2004

=> eqis

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EGIS IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s 369360-56-5/rn

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> file regis

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 19:08:52 ON 24 SEP 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 SEP 2004 HIGHEST RN 750479-89-1

DICTIONARY FILE UPDATES: 23 SEP 2004 HIGHEST RN 750479-89-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> s 369360-56-5/rn

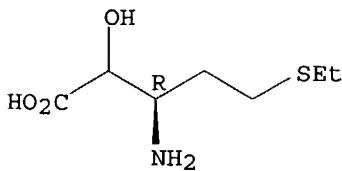
L1 1 369360-56-5/RN

=> d.11

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 369360-56-5 REGISTRY
CN D-glycero-Pentonic acid, 3-amino-3,4-dideoxy-5-S-ethyl-5-thio-, (2S)-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C7 H15 N O3 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d 111 sub bib abs
'111' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG	- RN
SAM	- Index Name, MF, and structure - no RN
FIDE	- All substance data, except sequence data
IDE	- FIDE, but only 50 names
SQIDE	- IDE, plus sequence data
SQIDE3	- Same as SQIDE, but 3-letter amino acid codes are used
SQD	- Protein sequence data, includes RN
SQD3	- Same as SQD, but 3-letter amino acid codes are used
SQN	- Protein sequence name information, includes RN
CALC	- Table of calculated properties
EPROP	- Table of experimental properties
PROP	- EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS	-- Abstract
APPS	-- Application and Priority Information
BIB	-- CA Accession Number, plus Bibliographic Data
CAN	-- CA Accession Number
CBIB	-- CA Accession Number, plus Bibliographic Data (compressed)
IND	-- Index Data
IPC	-- International Patent Classification
PATS	-- PI, SO
STD	-- BIB, IPC, and NCL
IABS	-- ABS, indented, with text labels
IBIB	-- BIB, indented, with text labels
ISTD	-- STD format, indented
OBIB	----- AN, plus Bibliographic Data (original)
OIBIB	----- OBIB, indented with text labels
SBIB	----- BIB, no citations
SIBIB	----- IBIB, no citations

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The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.

The MAX format is the same as ALL.

The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

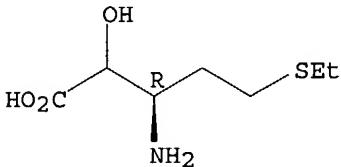
HELP DFIELDS -- To see a complete list of individual display fields.

HELP FORMATS -- To see detailed descriptions of the predefined formats.

ENTER DISPLAY FORMAT (IDE):ide

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 369360-56-5 REGISTRY
CN D-glycero-Pentonic acid, 3-amino-3,4-dideoxy-5-S-ethyl-5-thio-, (2S)-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C7 H15 N O3 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

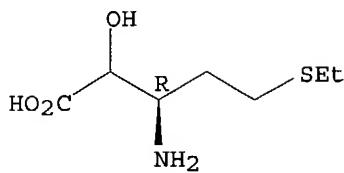
5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d 1 11 sub bib abs

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 369360-56-5 REGISTRY
CN D-glycero-Pentonic acid, 3-amino-3,4-dideoxy-5-S-ethyl-5-thio-, (2S)-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
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SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.

10458286



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 141:59732 CA
TI 3-Amino-2-hydroxyalkanoic acids and their prodrugs
IN Bamaung, Nwe Y.; Craig, Richard A.; Henkin, Jack; Kawai, Megumi; Searle, Xenia B.; Sheppard, George S.; Wang, Jieyi
PA USA
SO U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004122098	A1	20040624	US 2003-635342	20030806

PRAI US 2002-401317P 20020806
AB Compds. β -amino acid derivs. $H_2NCHR_1CH(OH)CO_2R_2$ [R1 = alkyl, alkylsulfanylalkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocycle)alkyl, hydroxalkyl; R2 = H, alkenyl, alkyl, alkylcarbonyloxyalkyl, alkylcarbonylalkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, heterocycle, (heterocycle)alkyl] or their therapeutically-acceptable salts are useful for treating conditions which arise from or are exacerbated by angiogenesis. Also disclosed are pharmaceutical compns. comprising the compds., methods of treatment using the compds., methods of inhibiting angiogenesis, and methods of treating cancer. Thus, (2RS,3R)-3-amino-2-hydroxy-5-(methylsulfanyl)pentanoic acid was prepared

REFERENCE 2

AN 140:164234 CA
TI Preparation of 3-amino-2-hydroxyalkanoic acids and their prodrugs
IN Bamaung, Nwe Y.; Craig, Richard A.; Henkin, Jack; Kawai, Megumi; Searle, Xenia B.; Sheppard, George S.; Wang, Jieyi
PA Abbott Laboratories, USA
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004013085	A1	20040212	WO 2003-US24396	20030805

W: CA, JP, MX
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
PRAI US 2002-213655 20020806
AB β -Amino acid derivs. $H_2NCHR_1CH(OH)CO_2R_2$ [R1 is alkyl, alkylthioalkyl,

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aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclalkyl, or hydroxyalkyl; R2 is H, alkenyl, alkyl, alkylcarbonyloxyalkyl, alkylcarbonylalkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, or heterocyclalkyl] or their therapeutically-acceptable salts were prepared for use in treating conditions which arise from or are exacerbated by angiogenesis. Pharmaceutical compns. containing these compds. are used in methods for inhibiting angiogenesis and treating cancer. Thus, (2RS,3R)-3-amino-2-hydroxy-5-(methylthio)pentanoic acid was prepared from Boc-D-Met-OH (Boc = tert-butoxycarbonyl) by reduction with sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al), oxidation of the formed hydroxymethyl group with sulfur trioxide pyridine complex, reaction with KCN and in situ hydrolysis of the cyanohydrin with 12 M HCl.

REFERENCE 3

AN 139:2799 CA
TI Physiologically Relevant Metal Cofactor for Methionine Aminopeptidase-2 Is Manganese
AU Wang, Jieyi; Sheppard, George S.; Lou, Pingping; Kawai, Megumi; Park, Chang; Egan, David A.; Schneider, Andrew; Bouska, Jennifer; Lesniewski, Rick; Henkin, Jack
CS Cancer Research, Advanced Technology, Global Pharmaceutical R & D, Abbott Laboratories, Abbott Park, IL, 60064, USA
SO Biochemistry (2003), 42(17), 5035-5042
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB The identity of the physiol. metal cofactor for human methionine aminopeptidase-2 (MetAP2) has not been established. To examine this question, we first investigated the effect of eight divalent metal ions, including Ca²⁺, Co²⁺, Cu²⁺, Fe²⁺, Mg²⁺, Mn²⁺, Ni²⁺, and Zn²⁺, on recombinant human methionine aminopeptidase apoenzymes in releasing N-terminal methionine from three peptide substrates: MAS, MGAQFSKT, and ³H-MASK(biotin)G. The activity of MetAP2 on either MAS or MGAQFSKT was enhanced 15-25-fold by Co²⁺ or Mn²⁺ metal ions in a broad concentration range (1-1000 μ M). In the presence of reduced glutathione to mimic the cellular environment, Co²⁺ and Mn²⁺ were also the best stimulators (.apprx.30-fold) for MetAP2 enzyme activity. To determine which metal ion is physiol. relevant, we then tested inhibition of intracellular MetAP2 with synthetic inhibitors selective for MetAP2 with different metal cofactors. A-310840 below 10 μ M did not inhibit the activity of MetAP2-Mn²⁺ but was very potent against MetAP2 with other metal ions including Co²⁺, Fe²⁺, Ni²⁺, and Zn²⁺ in the in vitro enzyme assays. In contrast, A-311263 inhibited MetAP2 with Mn²⁺, as well as Co²⁺, Fe²⁺, Ni²⁺, and Zn²⁺. In cell culture assays, A-310840 did not inhibit intracellular MetAP2 enzyme activity and did not inhibit cell proliferation despite its ability to permeate and accumulate in cytosol, while A-311263 inhibited both intracellular MetAP2 and proliferation in a similar concentration range, indicating cellular MetAP2 is functioning as a manganese enzyme but not as a cobalt, zinc, iron, or nickel enzyme. We conclude that MetAP2 is a manganese enzyme and that therapeutic MetAP2 inhibitors should inhibit MetAP2-Mn²⁺.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 4

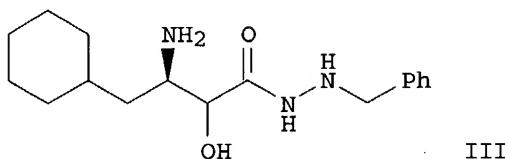
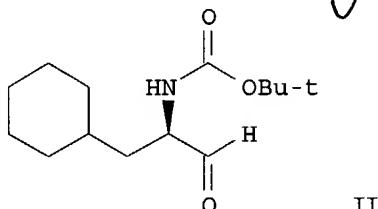
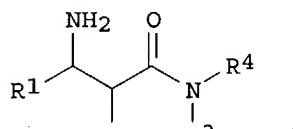
AN 136:69597 CA
TI Synthesis of hydrazide and α -alkoxyamide angiogenesis inhibitors
IN Craig, Richard A.; Kawai, Megumi; Lynch, Linda M.; Patel, Jyoti R.; Sheppard, George S.; Wang, Jieyi; Yang, Fan; Ba-Maung, Nwe

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PA USA
SO U.S. Pat. Appl. Publ., 78 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002002152	A1	20020103	US 2001-833917	20010412
	US 2004167126	A1	20040826	US 2004-782502	20040219
PRAI	US 2000-197262P	20000414			
	US 2001-833917	20010412			

GI



AB Title compds. I [R1 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocycle)alkyl, R5S-alkylene; R3 = H, alkyl, arylalkyl; R4 = NR6R7, OR8; R5 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl; R6-7 = H, alkanoyl, alkenyl, alkenyloxyalkyl, alkoxyalkyl, alkoxy carbonylalkyl, alkyl, alkylthioalkyl, aryl, arylalkanoyl, etc.; or R6-7 together are arylalkylidene; or R6-7 together with the nitrogen atom to which they are attached, form a heterocycle; R8 = H, alkanoylalkyl, alkenyl, alkoxy carbonylalkyl, alkyl, amidoalkyl, aryl, arylalkyl, etc.; R9-10 = H, alkyl, aryl] were prepared. Over 450 synthetic examples were reported. For instance, (2R)-2-(Boc)amino-3-cyclohexylpropanoic acid was reduced to the corresponding alc. (PhMe, Red-Al, 0°C, room temperature 1 h) and oxidized to II (DMSO, Py•SO3, Et3N, room temperature 30 min). II was converted to the bisulfite addition product

(H2O, NaHSO3, 5°C, 24 h) and reacted with KCN to give the α -hydroxy nitrile intermediate which was hydrolyzed to the carboxylic acid (12 N HCl, reflux, 21 h) and converted to III by condensation with benzylhydrazine (DCM/DMA, DIC, NMM, HOBT). Selected compds. I had IC50 < 0.1 μ M for MetAP2. I are useful for inhibiting angiogenesis.

REFERENCE 5

AN 135:331197 CA
TI Synthesis of hydrazide and α -alkoxyamide angiogenesis inhibitors
IN Craig, Richard A.; Kawai, Megumi; Lynch, Linda M.; Patel, Jyoti R.

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Sheppard, George S.; Wang, Jieyi; Yang, Fan; Ba-Maung, Nwe Y.
PA Abbott Laboratories, USA

SO PCT Int. Appl., 173 pp.

CODEN: PIXXD2

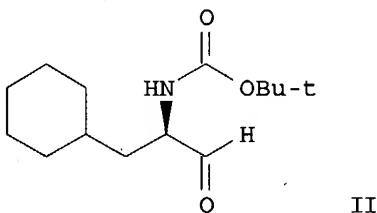
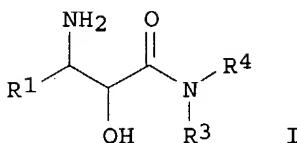
DT Patent

LA English

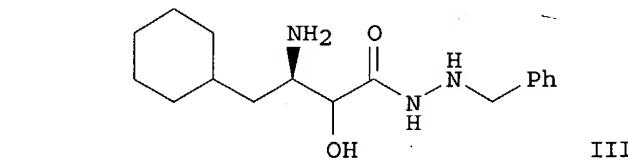
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079157	A1	20011025	WO 2001-US12274	20010413
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1272456	A1	20030108	EP 2001-925029	20010413
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	BR 2001007204	A	20040225	BR 2001-7204	20010413
	JP 2004509063	T2	20040325	JP 2001-576759	20010413
PRAI	US 2000-549995		20000414		
	US 2001-813008		20010321		
	WO 2001-US12274		20010413		

GI



W



AB Title compds. I [R1 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocycle)alkyl, R5S-alkylene; R3 = H, alkyl, arylalkyl; R4 = NR6R7, OR8; R5 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl; R6-7 = H, alkanoyl, alkenyl, alkenyloxyalkyl, alkoxyalkyl, alkoxy carbonylalkyl, alkyl, alkylthioalkyl, aryl, arylalkanoyl, etc.; or R6-7 together are arylalkylidene; or R6-7 together with the nitrogen atom to which they are attached, form a heterocycle; R8 = H, alkanoylalkyl, alkenyl, alkoxy carbonylalkyl, alkyl, amidoalkyl, aryl, arylalkyl, etc.; R9-10 = H, alkyl, aryl] were prepared. Over 450 synthetic examples were reported. For instance, (2R)-2-(Boc)amino-3-cyclohexylpropanoic acid was reduced to the corresponding alc. (PhMe, Red-Al, 0°C, room temperature 1 h) and oxidized to II (DMSO, Py-SO3, Et3N, room temperature 30 min). II was converted to the bisulfite addition product

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(H₂O, NaHSO₃, 5°C, 24 h) and reacted with KCN to give the α-hydroxy nitrile intermediate which was hydrolyzed to the carboxylic acid (12 N HCl, reflux, 21 h) and converted to III by condensation with benzylhydrazine (DCM/DMA, DIC, NMM, HOBt). Selected compds. I had IC₅₀ < 0.1 μM for MetAP2. I are useful for inhibiting angiogenesis.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT